Aus der Oto-Rhino-Laryngologischen Universitätsklinik Bern
(Vorsteher Prof. Dr. F. Escher)

ACUTE LARYNGOTRACHEOBRONCHITIS

A Clinical Study of 86 Cases Occurring During 1946-July 1954
At the University of Berne Hospital

INAUGURAL-DISSERTATION
zur Erlangung der Würde eines Doctor medicinae
der Universität Bern

vorgelegt von
ABRAHAM SHULMAN
von New York
(U. S. A.)

VERLAG P. G. KELLER - WINTERTHUR 1956

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I. Introduction

The purpose of this paper is to study the anatomical, physiological, clinical, epidemiological, and patho-anatomical material as presented in a series of eighty-six cases of laryngotracheobronchitis occurring in Berne during 1946 — July 1954. In our discussion special emphasis has been placed on a group of twenty-eight (28) cases designated as severe, twenty-five (25) of which required tracheotomy and three (3) that died under conservative management. All these severe cases (28) occurred in children ten years of age or under. The eighty-six laryngotracheobronchitis cases have been grouped into two categories: a smaller series of seven cases, consisting of five cases over the age of ten years of age, one diphtheritic LTB, and one case of obstructive thymus enlargement; and a larger series of seventy-nine cases consisting of the severe and non-severe cases in children till ten years of age. Our study concerns itself with this larger group.

At Berne we understand laryngotracheobronchitis clinically as a general acute infectious non-diphtheritic, obstructive inflammation of the lower respiratory tract. This may vary in the location and degree of maximum involvement, yet at all times it involves the larynx, trachea, and bronchi. This concept is based on the fact the entire lower respiratory tract is affected by a lesion in any one of its parts, regardless of the degree of intensity or localisation of the affection. The unit is a reflection of the function of its components and their change(s). Cases of acute laryngotracheobronchitis (aLTB) having the chief site of involvement in the larynx are designated as laryngeal (LA) laryngotracheobronchitis; in the trachea as laryngotracheal (LT) laryngotracheobronchitis; diffuse, equal involvement, as laryngotracheobronchial (LTB) laryngotracheobronchitis. In all cases the larynx, trachea, and bronchi are involved, but in varying degrees.

In the literature mention is made of the similar symptomatology presented by the non-diphtheritic obstructive affections of the larynx, trachea and bronchi. These non-diphtheritic obstructive conditions of the lower respiratory tract include:

1) Acute supraglottic edematous laryngitis (acute epiglottitis; influenzal laryngitis; inflammatory edema of the glottis).
2) Acute laryngotracheobronchitis (subglottic laryngitis; non-diphtheritic croup; virus croup).
3) Angioneurotic edema (supraglottic allergic edema).
4) Subglottic allergic edema (spasmodic croup; spasmodic laryngitis; false croup; catharral spasm of the larynx).

5) Foreign body in the larynx or trachea.
6) Related conditions — sudden death in infants; laryngomalacia, struma intratrachealis; enlarged thymus.

Each of these conditions may present themselves with evidence of acute obstructive dyspnea. We feel that greater emphasis should be placed upon a clinical thinking of all these conditions as an actual or potential aLTB, especially since a sharp differentiation according to the precise nature of the involvement — be it inflammatory or not — in a given case is not always a simple matter. Each of these forms of acute laryngeal obstruction causes the classic symptoms of laryngeal dyspnea. However, the urgency of the treatment and the type of treatment depend on the disease present. Prompt and accurate diagnosis is imperative, although difficult.

II. History of Acute Laryngotracheobronchitis

The history of aLTB includes the presentation of many different clinical concepts and classification systems, which reflect the uncertainty of the etiological factor or factors involved.

Blaud and Trousseau discussed aLTB one hundred years before the discovery of the diphtheria bacillus.

Mac Cready in a detailed report on the history of aLTB refers to two periods of development. He also mentions the multiplicity of terms and change of concepts of aLTB since the pandemic of influenza in 1918. In brief, the first period (1918—1938) is distinguished as the surgical or laryngological period. The acute obstruction, with therapy directed to the relief of the initial and recurring obstruction, placed the disease in the realm of the laryngologist. Supportive therapy was mentioned but not stressed. The term fulminating was applied to describe the clinical course. Etiologically, some cases were recognized as possibly representing a phase of an upper respiratory infection, varying yearly in incidence and severity. Major work was contributed in the United States by *Jackson, Neffson, Baum, Smith, Richards and Gittens.* Acute laryngotracheobronchitis was considered basically as an acute infection affecting the larynx, trachea, bronchi and the bronchioles with characteristic high fever, and glue-like exudate or secretion, partially or completely occluding the airways. Pathologically, it was unwise to refer to any of these cases, severe or mild, as a simple laryngitis.

The second period, the pediatric period, is stated to extend from the year 1938 to the present. Here the pediatrician, laryngologist, chemotherapy and antibiotics, play important roles. Supportive therapy which formerly was given secondary importance assumed prominence. Acute

laryngotracheobronchitis was established as a clinical entity, corroborating the pioneer wirk of *Jackson.*

Orten indicated that from 1918—1941, over three hundred cases had been reported in which the condition was so severe that the patients required hospitalization.

Halbertsma has proposed considering the non-diphtheritic obstructive conditions of the lower respiratory tract as a series of variations of one disease entity, consisting of the benign supraglottic laryngitis, mild subglottic laryngitides, severe stenosing subglottic laryngitis (laryngite stenosante), and the severest form acute laryngotracheobronchitis. It is of interest at this point, that the patients of Mac Cready's series which were considered aLTB died from a profound inflammation of the glottis which presumably extended to the trachea and bronchi. The interrelationship between the various non-diphtheritic obstructive conditions is evident.

Le Mee in a review of the French literature mentions *Lesne,* who observed cases during a severe grippe epidemic; *Bloch,* who reported cases in connection with an influenza epidemic; *Guillmot,* who stressed the importance of the tracheobronchial hypersecretion; *Coffin,* who used an antispasmodic, and *Halle,* who used an antispasmodic and antipyrin, both with favorable results.

The literature of the past ten years has dealt chiefly with treatment, and etiological classification. There is a relative absence of discussion concerning a clinical integration of the clinical entities involved.

In summary, our conception of aLTB is a clinical one based on the clinical observation of cases of non-diphtheritic inflammatory obstruction of the lower respiratory tract. Our cases indicated as (LTB) acute laryngotracheobronchitis are understood by the majority of authors of the literature as cases of the clinical entity acute laryngotracheobronchitis.

III. Anatomic Considerations

The following anatomical and physiological considerations found fundamental application in the clinical course of the cases of our series: —

a. Size of larynx — so small is the triangular aperture of the infant larynx, that an edema of one mm. of the mucosal surfaces of the glottic portion would reduce this area from 14 sq.mm. to 5 sq.mm., or to only 35% of the original area. The result would be respiratory change and obstruction. Aiding the edema spread would be the softness of the cartilages, greater compressibility of the walls, and the increased vascularity of the mucus membranes. A comparable amount of edema in the adult larynx would produce hoarseness. In our series, the majority of cases occurred in patients of age under one year till four years of age, with five of the eight deaths in patients of age under one year till two years of

age. The incidence, distribution and mortality of aLTB reflect the apparent importance of larynx size.

b. Mucosa anatomy of the lower respiratory tract: — the entire mucous membrane of the larynx is a ciliated pseudo-stratified columnar epithelium, except over the vocal cords where it is stratified and squamous in nature. The respiratory epithelium and mucous blanket of the nose and laryngotracheobronchial tree serve a specific function apart from that of the lungs, and should be considered vital to life, namely to conduct the inspired air to the alveoli and prepare it for use. The area of the lining epithelium increases markedly as the respiratory tract increases. When nasal function fails or is decreased the bronchiolar filter acts as an effective substitute.

The cilia increase up to the respiratory bronchioles where they already begin to decrease progressively and finally cease. An air conditioner exists which supplements and substitutes for the nasal function. Such a substitution surely occurs with tracheotomy. The fact that air flow decreases as the mucus blanket area increases further facilitates both deposition of suspended material and humidification. Destruction and decreased function of the respiratory epithelium, may well have been a contributing cause for the development and progress of aLTB in the overwhelming majority of cases who had a history of acute preceding upper respiratory infection, and in the case of complicating pertussis and measles.

The submucosa anatomy of the larynx finds particular application in our case originating as an epiglottitis with subsequent tracheobronchial involvement (LA). The mucous membrane of the larynx, with the exception of the posterior, laryngeal surface of the epiglottis and the vocal cords is not firmly bound down. Infection of the supraglottic area, as occurs in acute epiglottitis, produces an extreme inflammatory edema. An increase in the extravasated fluid results in expansion to the less adherent mucosa areas, namely anteriorly to the lingual surface of the epiglottis and laterally along the aryepiglottic folds, thus forcing the tip of the epiglottis backward, the edges inward, larynx closure, and the onset of symptoms of laryngeal obstruction. Immediately below the vocal cords, is located another mass of loose areolar tissue. Most acute obstructions are also predisposed to be localized in the subglottis since the edema of inflammation or trauma results in extravasation of fluid into the subglottic tissues with resultant increasing encroachment on the airway at its narrowest point. Edema causes further obstruction by limiting the mobility of the cords, preventing maximal abduction during deep respiration. Intimately concerned with the edema and infection spread is the lymphatic distribution. *Lüscher* mentions the importance of variation and the role of constitutional predisposition in the development of the mucosal lymphoid tissue. In reviewing the lymphatic distribution of the respiratory tract, the "Teichman Law" finds particular

application in the larynx, since if the extent of lymphatic development in an area depends on the amount of loose tissue present, then the entire larynx should be rich in lymphatics except at the points of maximal mucosal adherence. Such a point is the vocal cords, and here the lymphatics actually are absent. Lymphatic connection between the supra and infraglottic areas exists only at the narrow posterior interarytenoid area. The vocal cords thus form a barrier to lymphatic drainage of supraglottic edema to the infraglottic areas. The effectiveness of the barrier is affected by the virulence of the etiological agent as well as the constitution of the individuals. In our case of LA, the influenza virus was isolated. The high degree of viral virulence was instrumental in overcoming the "barrier", and extending the infection. In general, our severest cases involved the supra and infra glottic locations of profuse loose areolar tissue.

c. Cricoid cartilage — the structural rigidity given the subglottic area by the cricoid cartilage is unique since the cricoid is the only complete cartilaginous ring in the trachea. Whereas supraglottic edema may extend laterally into the soft pharyngeal tissues and become much more extensive before symptoms of respiratory obstruction arise, subglottic edema is limited in extension by the rigidity of the area. In two cases of LA the instrumental finding was more extensive than the symptomatology presented. *Neffson* cautions the physician concerning examination for supraglottic involvement and edema.

d. Constitution — the factor of constitution is an anatomico-physiological one. The role of constitution in aLTB must be considered *(Escher)*. The color of the respiratory mucosa, although influenced by the tissue thickness, vascularity, and superficial geography, has been shown to vary in different individual constitutional types. Ten of our serious cases revealed some constitutional information (tab. 1): four cases (one LA, no. 76; one LT, no. 33; two LTB, no. 58, 61) were of pasty, fair-haired, delicate appearance; three cases (one LA, no. 79; two LTB, no. 60, 73) were muscular, rosy complexion; one case (LTB, no. 63) was of pasty, nervous, delicate appearance; one case (LA, no. 27) pasty, adipose; one case (LTB, no. 53) weak laryngeal structure. Although the information is scanty, it is interesting that the incidence of the pasty, fair-haired, delicate, nervous child was high. The lymphatic distribution has been cited as subject to constitutional variation. In a report of *Braulke* dealing with the infectious non-diphtheritic stenosing conditions of the trachea and bronchi, six LTB cases are presented, one of which was a complication of measles. He concluded that pasty, weak children of lymphatic constitution (presumably supported by history and autopsy findings of status thymicolymphaticus) are probably disposed to the affection. Investigation of a possible role in some aLTB of lymphatic tissue distribution, as an expression of adrenal cortical in-

sufficiency has been attempted in our series and is included in the epidemiological discussion.

IV. Physiological Considerations

The clinical course and symptoms presented in the serious aLTB cases have been summarized (tab. 1). A discussion of the clinical course in the light of the physiologic-pathologic processes operating shall now follow since their understanding is fundamental in our diagnosis and therapy. The literature was thoroughly investigated and the salient features have been included in this discussion. Clinically, human pulmonary function should be considered as consisting of ventilatory function and respiratory function. The ventilation phase occurs with the passage of air from the nose to alveoli, where diffusion and intra-alveolar mixing of residual and tidal air occur. The pulmonary or respiratory phase occurs with the actual gaseous exchange between the alveoli and the blood. Ventilatory function is not necessarily paralleled by alteration in respiratory function. The degree of damage to each may be considerably different. During the ventilatory phase, the condition of the conducting airways; stretch reflexes; chemoreceptors; nociceptive and proprioceptive reflexes; and voluntary control are operating. During the respiratory phase the number of functional units; partition permeability; carbonic anhydrase activity; gas laws; oxidation of hemoglobin are the functional factors. A guide to the degree of pulmonary function can be obtained by constant care and should stress the major importance of the respiratory phase and lesser importance of the ventilatory phase. Constant pre and post operative care was attended to all our cases and the changes of anoxia, cyanosis, pale cyanosis, and abnormal respirations, reflecting essentially the respiratory phase, were immediately noted and treated accordingly. *Gray* clearly explained the pathophysiological basis of the symptoms which we saw particularly well in our serious cases. The chief complaint of all our patients was an acute episode of dyspnea. This is recognized as the first physiological change occurring in simple degrees of respiratory obstruction. It reflects a reduction in the ventilatory capacity of the individual (liters of air breathed per minute). Changes of the ventilatory capacity depend on the location and degree of obstruction, and the degree of the resultant dyspnea becomes a reflection of that change. The second physiological change in respiration becomes that of hypoventilation, namely the failure of the ventilation to meet body requirements. This condition develops in stages corresponding to the increasing failure of the pulmonary ventilation to keep pace with the increased oxygen exchange. The first stage manifests itself with exertional dyspnea and progresses to the second stage of dyspnea at rest. In our serious

cases, the increase in severity of hypoventilation paralleled the increasing respiratory obstruction. The symptoms observed, especially the noting of the onset of pale cyanosis, are explained by the "trinity" of progressive chemical changes occurring in the blood. The word asphyxia, implying interference with both O_2 and CO_2 exchanges expresses this "trinity" of blood changes consequent to hypoventilation. In sequence, the "trinity" of blood changes are: hypercapnia; arterial anoxemia; and acidosis, produced as the resultant of hypercapnia and arterial anoxemia. In mild cases of obstruction of the tracheobronchial tree, the developing respiratory acidosis remains compensated by a reflex and physiochemical stimulation. When the obstruction becomes severe, the increasing anoxemia causes lactic acid production of the tissues, the sufficient accumulation of which produces a metabolic acidosis. The presence of both a respiratory and metabolic acidosis is a potentially severe form of acidosis. The cyanotic stage is passed. Therefore, in severe cases of respiratory obstruction, the condition is not one of mere simple anoxia with hyperventilation, acapnia, alkalemia, but rather severe anoxia, since the retained CO_2 adds to the destructive effects of asphyxia. In our severe cases, no signs of tetany were recorded.

The relation of the degree of change in blood composition to the degree of hypoventilation is different in simple uncomplicated respiratory obstruction and in severe respiratory obstruction with pulmonary complications. In simple, uncomplicated, respiratory obstructive cases with moderate hypoventilation (80% of normal), hypercapnia predominates over anoxemia; with more severe hypoventilation (50% of normal), there exists a readily tolerated anoxemia with no cyanosis, hypercapnia approaching the narcotic level, a respiratory acidosis; with severe hypoventilation, drastic changes exist in all three blood constituents. In our cases of severe respiratory obstruction wih pulmonary complication, the effects of inflammation and vascular intrathoracic changes are of prime importance in producing the "trinity" of blood changes. The inflammatory, progressive clinical course of our severe cases is again cited to support our clinical conception of aLTB. The increased respiratory rate associated with laryngeal obstruction caused desiccation of the secretions with further obstruction by crusting. The treatment for prevention and elimination of crust formation was followed in all our cases. Associated with increased secretions are the vascular intrathoracic changes caused by laryngeal obstruction. Increased negative pressure on inspiration, due to laryngo-tracheobronchial obstruction, causes extravasation of fluid in the airway, increase to the secretions already present, pulmonary edema, suppuration, and finally, circulatory failure. Therefore, in cases of respiratory obstruction with pulmonary complications, the blood composition reflects a greater change with varying degrees of hypoventilation than in the cases of simple obstruction. The infection, edema, scattered areas of emphysema or atelec-

tasis, partial blocking of bronchi or bronchioles, explain the intensifying hypercapnia, anoxemia and acidosis of our severe cases. All the "trinity" factors are of prime importance. At Berne the degree of restlessness, distress, apprehension, disorientation, convulsions, and cooperativeness of the patient is constantly observed. They may be due to cerebral oedema or hemorrhages following prolonged anoxia, alkalosis, hyperpyrexia, air hunger. All our serious cases showed such symptoms. *Gray* believes these symptoms to be attributable to hypercapnia more than anoxemia. He notes that hypercapnia is as distressing as anoxemia is symptomless. Therefore in asphyxia, although the effects of anoxemia are severe, they only represent one third of the potential danger.

The therapy must attempt to increase primarily the respiratory function, relieve the respiratory obstruction and maintain an airway. Oxygen relieves the arterial anoxemia but does not improve necessarily the hypercapnia, acidosis or secondary pulmonary complications. Repeated tracheobronchial aspiration of secretions and crust removal, bronchoscopies, maintainance of electrolyte balance, stimulants, chemotherapy and provision of cool moist air were the essentials of our therapy.

Any respiratory obstruction carries with it the potentiality of reaching the critical phase of weakened respiration and fulminating asphyxia. All our serious cases showed a stage of "crisis". Clinically, the phase of stimulated breathing attributable to increased CO_2 concentration is scarcely seen in the child. The continous and rapid development of the succeeding phase of progressive anoxemia and acidemia, depresses the respiratory centers. As the breathing effort decreases, the adverse effects are intensified; a rapid end of breathing results. The danger of prolonged conservative management is great. It is evident that operative intervention must occur before the reserves of the patient are exhausted, if a therapeutic value is to be obtained from the procedure. Furthermore, the administration of sedatives must be done with great care.

Recorded evidence of breathing arrhythmia was found in five of our severe cases (three LTB; two LA). For a few hours immediately following tracheotomy there was a partial and sometimes momentary complete apnea. It is explained as a sudden depression in the respiratory center sensitivity produced by the sudden decrease in CO_2 level following tracheotomy. The severity was such that artificial respiration was resorted to in four cases. The remaining case showed Cheynes-Stokes respiration with progressive improvement.

An evaluation of the severe cases is now in order.

V. Clinical Course

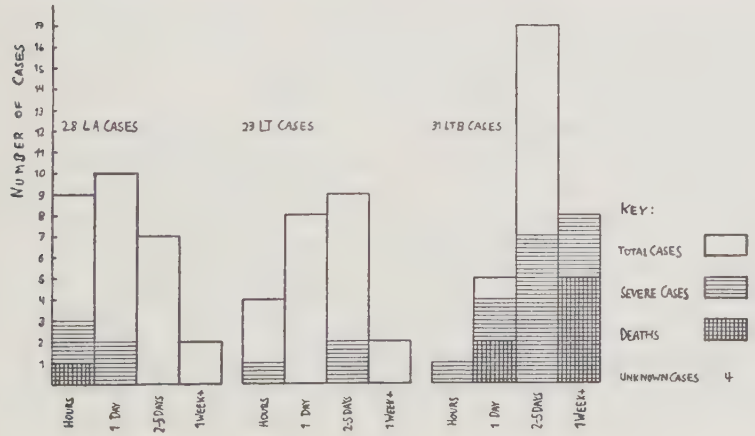
Emphasis has been placed on the severe cases and a summary of their histories is included (tab. 1). The following discussion deals with the studies of features of the clinical course of the serious cases, unless stated otherwise. The chief mode of onset of aLTB in Berne is of two main types. One type consists of an acute, sudden onset of respiratory difficulty with no history of past or present illness. The second type is characterized by an acute to moderately progressive onset of respiratory obstruction with a history of present and/or past upper respiratory infection. In general, these two main types of modes of onset are a reflection of the two main aLTB forms found in our series, namely, LA and LTB cases respectively.

Regardless of mode of onset, the clinical course is one of a rapidly progressing respiratory asphyxia with croupy cough, dyspnea, restlessness, temperature rise (37-40° C), pulse rise, pulmonary findings, inspiratory and also expiratory stridor, thoracic retractions, an initial stage of cyanosis with later pale cyanosis, circulatory collapse and death. Such a syndrome was also encountered as a complication of pertussis, measles, and a streptococcal sepsis.

Based on sixty-eight cases, with emphasis on the twenty-eight serious cases, the onset of the primary acute emergency to the time period of the day showed a high incidence of occurence between the late evening to dawn hours. No relationship was noted between the form of aLTB involvement to time of day onset.

Table 3:

Distribution of case forms of aLTB among the various time intervals:



The relationship which exists between the LA, LT, and LTB forms of aLTB (and which forms the basis of our clinical concept of aLTB) is clearly shown in tab. 3. Similar features can be noted in the graphs of the aLTB forms which were obtained by plotting the number of the respective cases, both mild and severe, against the time interval that elapsed between the onset of the acute episode and hospitalization. In reviewing the graphs one can conclude: —

1) The anatomical structures of the upper and lower respiratory tract is of basic importance in aLTB. The chief site of involvement is of paramount importance in the rate of development of the acute symptomatology. The pathophysiological relationships of the respiratory tract explains the greater incidence of LTB cases in the longer time intervals (2—5 da), prior to hospitalization, as compared to the LA cases (hrs.—1 da). It is known that in the LTB form the pathological change is accompanied by a gradual clogging of the lower trachea and bronchi. This would decrease the ventilatory and respiratory components of respiration, but at a more gradual rate than occurs in the sudden oedematous supraglottic closure in the LA form. Consequently, the LA cases show the greater incidence in the shorter time intervals. Furthermore, the LTB graph shows that although the larynx remains relatively more open than in the LA form, despite the more gradual course, the danger of the process is very great. This is reflected in the greater number of severe cases present in the longer time intervals of the LTB as compared to the LA, and LT forms.

2) The distribution of the LT and LTB forms in the early time intervals show a greater similarity than that of the LA cases. They vary only in number. Substantiation is found for the clinical difficulty actually encountered in the early diagnosis, particularly between the LT and LTB forms, and less so between the LA and LTB forms. This supports our clinical concept of considering, particularly early in the diagnosis, all the non-diphtheritic inflammatory obstructive infections of the lower respiratory tract as an actual or potential aLTB.

3) The incidence of cases in the longer time intervals increased as the chief site of involvement changed from the LA to LTB localization. This has already been explained on a primary pathoanatomicophysiological basis. Should this be the case, then similar, identical etiological agent(s) could produce the variations in the clinical pictures of our cases merely on the basis of variations in the site of chief involvement. Furthermore, whereas the similarities between the LA, LT, LTB graphs could be a reflection of similar etiological agents, the differences, particularly the greater incidence in the longer time intervals of the LTB cases could represent the operation of multiple or varied single etiological agent(s). However, if these different clinical courses, as reflected in different forms of aLTB and their graphs bear a direct or indirect relationship to different

or similar etiological factors must remain, on the basis of this study, an open but still a definite question.

The importance and relation of the symptomatology of gastrointestinal disturbance in the form of aphagia, diarrhea, vomiting to the acute episode and clinical course was attempted. Seven of our severe cases showed such symptoms. The autopsy of two cases (no. 58, no. 61) revealed edema and congestion of the gastrointestinal and abdominal organs. It appears on the basis of a small number of cases, particularly in the LTB form, that in addition to the chief symptomatic trias of cough, hoarseness and dyspnea, evidence of gastrointestinal dysfunction should be looked for and evaluated as possibly a sign of the degree of the developing toxic state. Similarly on the basis of the physiologic considerations presented, blood chemistries would be of value in following the clinical course.

A survey of the incidence of *repeat attacks* revealed involvement in ten cases of the total series, including four severe cases. Three severe cases showed an initial attack of LTB, of which two cases later developed two succeeding episodes of LA (no. 36, no. 39) and one another episode of LTB (no. 75a). The remaining severe case presented an initial episode of LT and later LTB (no. 77). One of the repeat severe cases (no. 75a) revealed a history of repeated angina and breathing difficulty since birth. It is noted that despite repeat attacks no case was tracheotomized more than once.

The *family history* revealed no real difference in the relation of the amount of previous infection in the family to family size. One should think that the probability of acute respiratory obstruction, especially if assumed or accepted to be of infectious origin, would not only be greater in larger families, but that evidence of previous infection would also be greater. Both these points were found, however, to be true in only a few cases. It may well be, that the infectious nature of the process plays the primary role in these positive cases. No relationship was found between the disease incidence and social standing of the family.

The complications of our serious cases were studied. Twelve cases showed complications, of which ten had been tracheotomized. This group included seven of the eight deaths in our total series. LTB was the form of aLTB in nine cases. The remainder include bronchiolitis one case, and LA two cases. The most frequent complications were found to be bronchopneumonia, emphysema, sepsis, and encephalitis. The two cases of sepsis include one of definite streptococcus origin; the remaining case of possible pneumococcus origin. Breathing arrythmias have been mentioned. The complications of tension pneumothorax and mediastinal emphysema were not found. It is noted that the complications in our series are a reflection of the obstruction syndrome, presented by all aLTB cases.

The essential features of the *diagnosis* consist in the recognition and proper evaluation of the history and symptoms of the respiratory obstruction plus the localisation of the chief site of obstruction. In addition to the physiologic considerations already presented the following elaboration deserves mention. The cyanosis of rather sudden laryngeal obstruction is self-evident and measures are immediately taken to relieve it. The pale cyanosis, with restlessness, high fever, dehydration and weak pulse are symptoms consistent with obstruction and prompt therapy must be initiated. The latter state lacks the dramatic quality of the livid cyanosis, but are severe, since they are considered secondary to toxemia due to the severe pneumonic infection.

The differential diagnosis includes the already mentioned non-diphtheritic obstructive conditions affecting the lower respiratory tract, pneumonia, as well as laryngeal diphtheria. In our series the chief differential exists between the LTB and the LA forms of laryngotracheobronchitis and diphtheritic laryngotracheobronchitis.

VI. Laboratory Findings

The laboratory findings of the urine, blood, and bacteria were investigated. The inadequate number of cases with urinanalyses prevented the formation of any conclusion concerning the urine findings. Analyses of the blood and bacteria findings were made.

A. Blood Analysis

In our series a total of fifty-nine cases, including eighteen serious cases presented blood examinations for evaluation. The cases were analysed to see the relationship, if any, between the clinical picture of LA, LT, and LTB and their respective blood picture. For this analysis, the time period between the initial onset of the illness to the removal of blood for examination in the hospital was recorded. In this manner, an attempt was made to determine the original reaction of the blood to the infection. In the analysis, I assumed that the disease process, specifically bacterial infection, would reflect its course in the blood with characteristic changes. The labile state of equilibrium shown by the hematopoietic system, which decreases with increasing age, was taken into consideration in the analysis.

Our blood findings revealed: —

1) The red blood cell changes were few. The total incidence of RBC change, as reported in our series, was too small to allow any definite conclusion to be made.

2) The blood changes were most manifest in the total and differential white cell counts. On the basis of the variations of the total white cell

counts in all the cases analysed, four main groups of total white cell count reactions exist: —

a. Group I — Cases with a normal total white cell count.
b. Group II — Cases with a reactive leucocytosis.
c. Group III — Cases with a reactive leucopenia.
d. Group IV — Cases with a reactive leucopenia and absolute lymphocytosis, followed by a neutrophilic leucocytosis.

The largest number of cases occurred in Group I and II. The results of the serious cases are included in their summary (tab. 1).

3) Analysis of the differential white cell blood counts revealed the most frequent changes to be: —

a. Toxic granulations of the neutrophiles.
b. Lymphocytes — relative and absolute lymphocytosis.
c. Eosinophiles: — a slight eosinophilia in LTB and LT cases, either accompanying a reactive leucocytosis or leucopenia.

4) The total leucocyte counts showed a wide variation from 4000 to 35 000. A definite relationship exists between the blood count and the day of the illness.

Interpretation of the blood findings was considered of value in relation to the clinical course and bacteriological findings. The following conclusions were made: —

1. A majority of all forms of aLTB showed a reactive leucocytosis. This is interpreted as an expression of the secondary infection produced by the similar bacteria recovered from the majority of aLTB cases.
2. Based on the total series, the LA and LTB forms showed a proportionately greater number of normal and leucopenic reactions than did the LTB form. Based on the serious cases, the LT and LTB forms showed the proportionately greater number of normal and leucopenic reactions. The importance of viral etiology and the effect of antibiotic therapy should be considered.

Clinically, no association was found between an aLTB form and a particular blood picture. Etiologically, however, the variation in the distribution of the total and differential findings among the different aLTB forms, when considered together with the history, course and bacteriological data of a particular aLTB form, supports a contention of multiple factors operating in aLTB.

B. Bacteriology Analysis

The diversity of the bacteria (tab. 4) was determined in a total of thirty-five cases, including nineteen serious cases. Streptococcal infection was found to have the greatest incidence of occurrence in LA, LT, LTB. It occurred as an accompaniment of a mixed infection in the great pro-

portion of all our cases, and was only considered in single cases as the probable primary cause of the disease. In general this is in keeping with the character of the streptococci, which show perhaps a greater variety of diseases of man than any other kind of bacteria. In addition to occurring as the primary cause of a disease, mixed and secondary infection with other pathogenic agents are produced. In our series the H. influenzae was not found. Its absence is possibly explained by its extreme sensitivity to noxious stimuli with resultant death prior to the cultivation of the obtained material. The remaining bacteria reported are mainly those found in secondary infection(s). The green-producing streptococci showed a high degree of incidence in our cases as did *Heatly's* cases. An analysis of the cases in which it was found supports the contention of its role in secondary infection. It is noted that no correlation exists between the particular clinical course (LA, LT, LTB) and the reported bacterial flora. A similar bacterial flora was reported in all cases. This supports a contention of the secondary nature and secondary importance of the bacteria usually found in aLTB cases. It now becomes apparently clear why the total and differential white cell counts in the majority of our cases revealed the predominant changes of a reactive leucocytosis.

Viral investigation in our series was initiated in February, 1954. (Bacteriology Institute, Prof. Hallauer, University of Berne.) Since then, four cases of our series and one case in December 1954 were investigated. Influenza virus A has been isolated by *Loeffler* from one case (no. 76) of acute epiglottitis progressing to aLTB, and in a second case not included in our series (Dec. '54). In the two other cases of this period, the antigen test was positive. The remaining case of our series was fatal and revealed no virus. Although the virus isolation case of our series is considered of primary virus etiology, the clinical picture is believed to be one of superimposed secondary infection. Examination of the blood reactions in our cases showed the typical virus reaction in the blood, of an initial leukopenia with absolute lymphocytosis followed by a neutrophilic leucocytosis, to be infrequent. The blood picture of our virus case, examined two days after the acute onset, showed a reactive leucocytosis. Some of our cases are possibly either of primary virus infection with the predominance of secondary infection, or have other etiological factor(s) operable. In relation to our virus investigation, the procedures involved are costly, difficult and time consuming. These factors prevented the routine examination of all our cases for a virus. Despite these limitations the virus and corresponding serological reaction has been demonstrated at Berne in the limited number of cases investigated. This evidence supports a thesis of the primary role of a virus in infectious aLTB. Furthermore, the remaining reported bacteria should be considered as secondary agents of infection. The possible secondary role of the virus in infection is considered improbable since a completely developed influenza virus

usually possesses sufficient virulence to cause an immediate disturbance *(Loeffler)*. It cannot be stated how long the virus was present in the patient before the acute onset commenced. These conclusions are considered definitely valid in the virus case. A generalisation of viral infection for all aLTB cases based on so minimal an amount of material should not be made.

I have found on the basis of history, blood and bacteriology, and clinical course studies that multiple agents, acting alone or in combination, are operative in LA, LT, LTB. They can be categorized as primarily infectious or primarily constitutional determining infectious agents. Specifically, if the etiological conception of aLTB is considered in most cases to be that of infection with the influenza virus, then the course and the resultant clinical picture is determined in a large degree by the constitution and reactive condition (specifically hypersensitivity) of the patient. In some aLTB cases, particularly the severest, it is possible that the role of the constitutional and reactive factors are of paramount importance, in the sense of an Adaptation Failure. That is, a primary constitutional determining aLTB. This is a clinical pathophysiological concept. It is offered as an addition to the classical anatomical considerations presented by age in the etiology of aLTB. I consider of diagnostic importance, the positive indication in our series of the activity of multiple agents in the production of aLTB. The difficulty at the onset of the diagnosis is believed due to the failure of distinguishing between the clinical and etiological (multiple) aspects of the diagnosis. At the onset, the problem is primarily clinical rather than etiological. Our concept of aLTB, a clinical one, should prove of diagnostic aid. In all our cases, particularly the LA forms, the infectious etiology was paramount. However, the primary constitutional determining aLTB cases increased in the aLTB form. *Rabe* has recently presented an etiological classification of croup, which can be considered the etiological adjunct to our clinical concept of aLTB.

VII. General Epidemiological Information

Sufficient general epidemiological information was found in our entire series. The distribution of aLTB was determined in children ten years of age or under (tab. 5). The maximum incidence was found between the ages of 1 to 4. A poorer prognosis and greater severity was found in the younger children and infants. The distribution of total cases among the sexes was slightly greater in the male than female. However in the severe cases, the distribution was practically equal. The distribution of deaths was equal in the male and female, but the percent mortality slightly

higher in the female than the male. The geographical origin of our cases was rural in 49 cases, urban in 31 cases, and 6 cases were undetermined. The serious cases revealed 15 rural, 12 urban cases, and 1 case undetermined. In both categories of the series the rural areas show a slightly greater incidence. However, 6 deaths were of urban origin and only 2 deaths of rural origin. The infectious nature of aLTB has appeared in the form of epidemics in both Australia, Puerto Rico, and Canada. In our series, there is an apparent regular number of acute obstructive laryngeal respiratory conditions occurring each year (tab. 2a). The larger number in 1951 possibly represents the increased incidence of grippe in that year. *Orton* and *Gilbert* also noted an increase in their cases during 1939—1940, and mentioned the possible relation to the grippe epidemic. In view of our study and the literature, the isolation of the A influenza virus from one of our cases is of great etiological interest, particularly to our other aLTB cases. The cases were distributed throughout the year (tab. 2b). The lowest incidence occurred during June to August; the peaks in November to February. A greater degree of increased case incidence was noted in a change from warm to cold weather than from cold to warm weather. The possible etiological factor of a physical agent (cold) acting initially alone and later in conjunction with an infectious agent must be considered. *Davison* mentions the relation of cold to cases of subglottic allergic edema. Perhaps some LTB cases are an extension of such an initial lesion. This is cited as support for the contention that multiple etiological factors exist in aLTB.

Tab. 5: Age Distribution

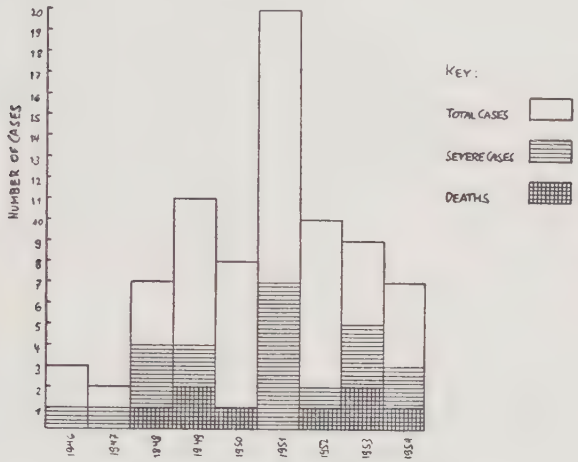
Age	Total Cases	Severe Cases	Deaths
Under 1	13	5	3
1—2 yrs.	22	9	2
2—3 yrs.	14	5	—
3—4 yrs.	19	7	1
4—10 yrs.	11	2	2
TOTAL:	79	28	8
Over 10 yrs.	7		

Tab. 6: Sex Distribution

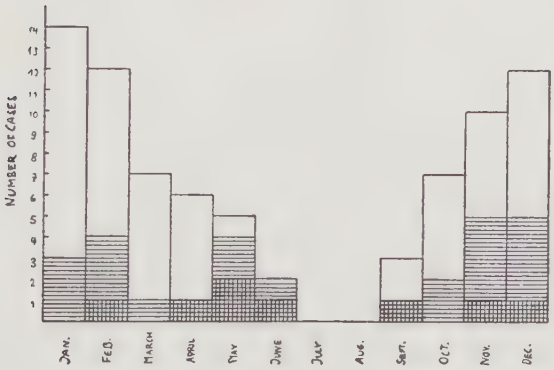
Sex	Total Cases	Severe Cases	Deaths
Male	54	15	4
Female	32	13	4
TOTAL:	86	28	8

Table 2:

a) Yearly incidence, distribution, and mortality of 79 cases of aLTB, including 28 severe cases



b) Seasonal incidence and mortality of 79 aLTB cases



An evaluation of the importance of the *carrier and vector* factors in our aLTB cases was attempted. Case number 56 is cited as an illustration. Twelve days prior to admission the patient visited his cousin, who showed the presence of a severe cough at the time. Two days following the visit, the cousin became ill with LTB. In our patient a similar onset of cough preceeded the acute symptoms, with LTB developing in the next two days. Both cases apparently parallel themselves in their development. The infectious transmissible nature of the process in this case seems evident. Furthermore, twenty-two cases of the entire series showed some history of recent family or community infection. They comprised five LA cases, including one serious case; six LT cases; eleven LTB cases; including eight serious cases. Two of the eight serious cases died. An increased incidence of recent illness in some LTB cases is noted. This result can be noted to support the contention that the multiple factors in aLTB increase in the order of LTB more than LT, which is more than LA. Of the total twenty-two cases: — sixteen had an illness in the immediate family affecting the portions of the respiratory tract; four had a disease in their community (diphtheria; catharrh; grippe) affecting the respiratory tract; and nineteen cases whose immediate family of community showed illness prior to their own, showed illness affecting predominantly the upper and lower respiratory tract. The probable etiology of the surrounding illness is explained in the literature as of viral origin. The virus may therefore be the chief etiological factor of the multiple ones advanced for the etiology of aLTB cases in Berne. Twenty-two cases of the total series, including eleven severe cases and three deaths, presented histories of no previous illness.

VIII. Mortality

A survey of the mortality was performed in our series and compared to the literature. Five of the eight deaths were in the tracheotomized cases. In this paper, no comparisons were made between the clinical course of the tracheotomized and non-tracheotomized patients. In Berne, tracheotomy is only resorted to when conservative therapy is of no further avail. *Escher* maintains that all cases in which tracheotomy upon the inserted bronchoscope was performed, would, if treated otherwise, have had a fatal course. The specific mortality rates of the seventy-nine cases of our series (tab. 3) showed the LTB forms to be the most fulminating, although the incidence of the LA form is slightly higher. The statistical comparison of the tracheotomized cases of Berne to the statistics of leading authors in the United States was of great interest (tab. 7). With the excepion of *Simpson,* some of whose cases were treated with anti-

biotics, the cases reported can be divided on the basis of therapy into the pre- and post-antibiotic era. The Berne cases comprise the antibiotic era. Their comparison to the literature reveals no remarkable effect of the new treatment. Simpson has a mortality of 18 ± % from 1940—47. However, during the years of 1946—47, three of the five tracheotomized cases died. The mortality difference is staggering. He notes that despite the favourable reports of the antibiotic influence on the mortality, all cases have not yet been brought under control.

It has already been mentioned that the degree of toxicosis, clinical form of aLTB and the reactive state of the patient can be of such importance that antibiotic therapy is of no apparent value. In order to compare the results of other authors with our own, an evaluation of the respective therapy regimens must be made.

IX. The Therapy

The therapy regimen at Berne as described by *Escher* is based on a fundamental knowledge of the pathologic changes associated with that disease. It includes treatment of the general and local disease factors present, namely the desiccation, toxicosis, dyspnea and anoxemia of the stenosing laryngobronchial system, as well as the impending circulatory collapse. General supportive measures include continuous fluid and electrolyte balance including infusions and percorten; maintainance of the patient in a humidified, cooled croup tent; treatment of the circulation with stimulants when needed. Local measures include laryngoscopy and repeated bronchoscopies through the tracheostoma when necessary to remove the crusts and excessive secretions within the tracheobronchial tree. The state of crusting may last 10 to 14 days in the absence of antibiotics. Intubation is not performed. Tracheotomy upon the inserted bronchoscope is performed in all severe cases with toxicosis and extreme dyspnea. Throughout the treatment penicillin, 300,000 units p.d. and streptomycin $^1/_4$—$^1/_3$ g. p.d. are used. *Escher* mentions the change in the clinical course of our cases as an accompaniment of the use of antibiotics. Previously the elimination of the secondary stage of crust formation extended from 10 to 14 days. Today the liquefaction of the secretion and crusts, aided by the instillation and suction of solutions through the cannula, occurs within days, and decannulation can follow in 5 to 8 days. In addition, the incidence of complications due to tracheotomy and decannulation(s) has become insignificant. The literature mentions the favourable action of terramycin, chloromycetin, aureomycin, and a wetting agent (Duponal C). The wetting agent prevented the drying of secretions, which *Baum* contends is aided by tracheotomy. It was added to the

Tab. 7: Statistical Comparison of the LTB Tracheotomized Case Mortality of Berne and that of the Literature:

Author	Tracheot.	Deaths	Tracheot. Mortality	Date
1. Gittens	15	8	53.0 %	1936
2. Smith	12	4	33.0	1936
3. Baum	13	8	61.0	1928
4. Richards	23	12	50.0	1937
5. Brenneman & Holinger	24	10	42.0	1936
6. Brighton	27	11	40.0	1940
7. Orton	20	77	35.0	1940
8. Felts	17	4	23.0	1940
9. Davison	99	1	11.1	1940
10. Simpson	64	12	18 ± %	1940—47
11. Berne	25	5	20.0	1946—54

TRACHEOTOMY ANALYSES

Tab. 8a: Incidence; Mortality:

aLTB Form	Cases	Deaths
LA	5	1
LT	3	—
LTB	17	4
TOTAL:	25	5

Tab. 8b: Time period between the initial attack of the respiratory distress to hospitalization and mortality, based on the tracheotomy cases:

Time Interval	LA	LT	LTB	Total	LA	LT	LTB	Total
Few hrs. — 1 day	3	—	8	11	—	—	2	2
1—2 days	2	1	2	5	1	—	—	1
2—3 days	—	2	3	5	—	—	1	1
3—4 days	—	—	1	1	—	—	—	—
5 days	—	—	3	3	—	—	1	1
TOTAL:	5	3	17	25	1	—	4	5

Tab. 8c: Time period between hospitalization to tracheotomy onset, and the mortality:

Time Period	LA	LT	LTB	Total	LA	LT	LTB
Immediately	1	1	8	10	—	—	3
Few hours	2	2	9	13	1	—	1
1—3 days	—	—	2	2	—	—	—
TOTAL:				25	1	—	4

moistened respiratory air and resulted in dramatic relief. This product is said to be non-toxic.

The treatment as presented in the literature is essentially similar. *Neffson* notes that in addition to the usual treatment the patients should have, if possible, a routine roentgenographic examination to determine the presence of pneumonia, atelectasis, pneumothorax, and mediastinal or pulmonary emphysema. *Davis* stresses the neglected use of hypertonic plasma solution. The administration of about 20 cc. intravenously results in a rapid and dramatic improvement. *Simmons* in discussing the preventive treatment of laryngotracheobronchitis in a child of 22 month, stresses the ruling out of allergy, especially to dust. Again evidence is found to support the existence of different types of LTB.

X. Tracheotomy Analyses

Tracheotomy forms an essential part of the treatment, especially in the severe cases. Our studies of the *tracheotomized cases* generally support *Escher's* statement that the absence of operative procedure in the severe cases results in a mortality of 100 %. A study of the incidence of tracheotomy and mortality (tab. 8a) revealed that 25 cases of the total series of 86 cases required tracheotomy. Of the total deaths in the series, five occurred with a tracheotomy. It appears that on the basis of a statistical interpretation, tracheotomy was of little value in this group. However if no tracheotomy were performed the effects of the obstruction would have produced exitus sooner. In any case, there appears in our series a group of cases of such severity as to overcome the therapy regimen and produce exitus. The time period between the initial attack of respiratory distress to hospitalization and the mortality involved (tab. 8b), revealed that the cases with the longer histories showed a lower mortality. The future prognosis of the LTB cases improves, but is still severe, as the history prior to hospitalization lengthens. Therefore, the high mortality of LTB is apparently limited to those LTB cases with an acute onset. This study and others already cited, indicates that the LTB form of aLTB, more than the LA and LT forms, is possibly initiated by a different factor(s). In contrast to the LTB cases, the fatal LA cases all present an acute history of onset of hours till two days prior to hospitalization. Therefore both the fatal LA and LTB cases with histories of acute short onset could have an identical etiological background with a possible direct relationship to the case of virus isolation.

In summary, the LA cases revealed a history of a few hours to two days between acute onset and hospitalization; LT cases, a history of 1 to 3 days; LTB cases a history of hours to more than 5 days between acute onset and hospitalization. A study of the time period from hospitalization

to tracheotomy and the mortality (tab. 8c), indicates that those patients needing tracheotomy showed indications for it either immediately or a few hours after admission, regardless of the chief form of aLTB involved. In the LTB form, the mortality was maximum in the cases tracheotomized immediately or a few hours after hospitalization. This was the period of maximum toxicosis.

On the basis of these studies the LA and LTB cases are the most severe cases of our series. The fact that a small group of cases died with tracheotomy is not attributed to the procedure, but rather to the degree of toxicosis, which was not apparently sufficiently influenced at the onset of the therapy.

The *antibiotics* bear special mention in our series. Reference has already been made to *Simpson's* statement that the disease in its fulminating form has not been brought under control in all cases, despite the favourable reports since the introduction of antibiotics. There are some cases which despite supportive, antibiotic, and operative procedures either end fatally, or have a "see-saw" clinical course. The lack of a relatively immediate response to the antibiotics in such cases, shows their secondary importance in the initial period. In such cases they are primarily supportive rather than combative. The response to the antibiotic components of the therapy regimen was of great interest in case no. 36a. At first penicillin and streptomycin were prescribed in high dosage. Concomitant with this initial therapy, a series of antibiotic resistance tests were performed on material obtained from the trachea. A more positive reaction to chloromycetin was noted and instituted accordingly. This change in the therapy was initiated after 5 days of hospitalization. The chloromycetin was applied for 4 days and resulted in a rapid fever decline after one day. Two days following the removal of the chloromycetin, a complicating bronchopneumonia developed. This can be cited as a case where the secondary infection dominates the clinical picture. Such was the explaination of the case of virus isolation. Chloromycetin, included in the broad spectrum antibiotics, was here active. In interpreting the importance of chloromycetin in this case, it must be kept in mind that many LTB cases show improvement after a time period corresponding to that in this case, without chloromycetin. In case no. 39a all of the broad spectrum antibiotics showed the massive positive reactions. The changing character of the bronchial flora was reflected in the second antibiotic resistance test performed 9 days following admission. It is therefore apparent that the changing character of the response of the secondary bacterial flora to the therapy is a factor responsible for the protracted course of the illness in some cases. An initiating but limited action of a virus with ensuing superimposed and predominating secondary infection was perhaps operating in this case. In this manner we could have a primary virus infection with an initial

reactive leucocytosis. This was the blood picture in the case of virus isolation.

In summary, the therapy is essentially the same in Berne as compared with the leading authors in the United States. I believe that the failure to eliminate aLTB in its severe form in all cases, despite antibiotic therapy, is explainable by: —

1) the different degree of toxic manifestations presented by the individual cases of the LA, LT, LTB forms of aLTB.
2) The paramount role in some aLTB cases (particularly the LTB form) of the already mentioned factors of constitution, disposition, resistance, and allergy. The primary constitutional determining infectious aLTB cases.

In the main, the therapy is primarily a supportive one directed against the toxemia, the impending circulatory collapse, and including antibiotics. In relation to the latter explanation (no. 2), the question concerning both a means of intensifying this supportive therapy and what the possible therapeutic effect would be, is of interest. Possibly the additional action of Cortisone in selected, severe toxic states, combined with intensive wide spectrum antibiotic therapy would produce a more favourable "adaptation" to the disease process. At present, no such individual experiences can be reported from Berne. Case no. 61 is cited together with the autopsy report as an example of a primary constitutional determining LTB form of infectious aLTB. Diagnosis based on clinical and etiological concepts and facts should possibly reduce the mortality, particularly of the LTB form.

XI. Pathologic-Anatomy Considerations

Our pathological-anatomy findings were observed both on autopsy (tab. 9), and during the course of the aLTB process (tab. 1). In our series the chief localisation of the pathology was in the supra- and subglottic areas. The LA and LTB forms of the aLTB predominate in both of the original categories of the series. Our discussion concerns itself primarily with these two forms. Other cases include the LT form of aLTB and one case of bronchiolitis. Regardless of the chief site of involvement, the larynx, trachea, and bronchi were involved. The pathological observations in our cases designated as the LA and LTB form of aLTB correspond essentially to cases in the literature termed acute epiglottitis and acute laryngotracheobronchitis, respectively.

In all our serious cases, the pathological lesions were the same. The difference lies in the site of chief involvement and in the degree of severity and degree of extension of the primary lesion into the adjacent areas. Basically the process is an acute inflammatory one of the larynx, trachea, bronchi, and bronchioles.

In the LA form, there is a marked swelling of the epiglottis and the aryepiglottic folds with less swelling of the ventricular bands and still less swelling of the true cords and tracheal mucosa. The epiglottis shows a marked edema; appears as a bright red cherry; submucosal round cell and leucocyte infiltration; as well as ulceration of the mucosa and fibropurulent formation(s). The inflammatory reaction of the larynx decreases from the epiglottis downward. *Gilbert* states that such patients rarely if ever show co-existing subglottic edema. He considers supraglottic edematous obstructive laryngitis (acute epiglottitis) to be a localized, self-limited inflammatory process. However, in our series, some cases showed a minimal inflammatory reaction subglottically, but others develop a diffuse involvement of larynx, trachea, and bronchi (tab. 1).

In the LTB form, there is found early, a thick larynx and absence of motion. There is a subglottic edema with an intense redness and velvety appearance. At the start, as in LA, the surface layer is intact (in contrast to the destruction of diphtheria); the submucosa edematous; dilated capillaries; and many leucocytes. The process advances into the subepithelial tissue with diffuse cellular infiltration and destruction of the surrounding walls. Fibrin and purulent exudate occludes the walls of the trachea, bronchi, and bronchioles. The secretion and activity of the glands is in contrast with the subnormal activity of the laryngeal and tracheal glands in diphtheria. The ropelike exudate and crusts consist of a mixture of mucus, fibrin, polymorphonuclear leucocytes and degenerated epithelial cells. The infection has an erysipelas-like character with invasion of the subepithelium, supraglottis and infraglottis. This type of infection predisposes to secondary infection which produces the destructive changes, exudate and necrosis. With the partial to complete obstruction of the bronchi, there developed in the lung the emphysema, atelectasis, and pneumonia of our series. *Orton* states that where the staphylococcus is present, there occurs early in the course of the infection a marked destruction of the mucosa and wall of the trachea with a formation of dirty, gray, thick, tenacious, mucus plugs, which dry and crust. This is a manifestation of the necrotizing character of the staphylococcus. In the presence of predominantly streptococci, this is frequent late in the course of the disease.

Exclusive of the upper respiratory and lung findings, autopsy (tab. 9) revealed changes of an acute infection in the myocardium, kidney, stomach, liver, spleen, and brain.

In relation to the factor of allergy, examination of the pathological material presented, revealed no evidence of definite allergic phenomena, to have occurred. Investigation of the history, physical examination, clinical course and routine laboratory procedures revealed no overwhelming positive evidence to support a contention of the presence and primary importance in aLTB of a different reactive state of the patient

(allergy) and a corresponding allergen. The performing of various allergen tests on the patients was not feasible. However, despite this lack of overwhelming positive evidence for allergy in our series, the lack of positive evidence against this thesis should still permit one to consider the role, if any, exerted by allergy in some aLTB cases. It is possible that there exist mixed forms of allergic glottic and subglottic edema in which the addition of an infectious factor produces the severe character of the disease.

Similarly, it was not considered possible, on the basis of case no. 27, to definitely determine the role, if any, exerted by the presence of Status thymolymphaticus in cases of aLTB. However, our observations agree with *Braulke* that pasty, weak children with a lymphatic constitution show a predisposition to aLTB. It can be said that the greater tendency for tissue swelling in the pasty habitus is probably of special significance in aLTB.

The formation of sticky and gelatinous crusts was of great concern in our series. *Baum* contends that their formation is to some extent aggravated by the air entering through the tracheotomy wound. While this does not usually occur in tracheotomized patients in the absence of acute infection, it might play a role in aLTB. Control of the secondary infection with antibiotics aided many of our cases.

Werne and *Garrow* have shown by histologic study that the occurrence of sudden death in infants (those infants found dead and those observed to die), who are in apparent good health and in whom gross necropsy findings were inconclusive, disclosed mainly significant disease of the respiratory tract. The absence of morphologic evidence of the systemic reaction (vascular or lymphatic tissue) as well as the low incidence of minor respiratory lesions in infants dying immediately after violence, is in sharp contrast to the histologic findings in infants dying suddenly while in apparent good health. This contrast established the pathologic significance of their gross and microscopic findings. With respect to etiology, the authors conclude that since the etiologic agents responsible for the great majority of respiratory diseases are unknown, it is not surprising that the specific causes for the fulminating respiratory disease in the infants found dead remain to be discovered.

In *Gruenwald and Jacobi's* study of two-hundred related cases of sudden death in infants, correlation of the clinical course with the pathologic findings suggested an infection of viral etiology in most cases. At autopsy a diffuse mononuclear pneumonia was frequently found. These patients were brought to the hospital acutely ill, with a cold, an upper respiratory infection or cough, diarrhea or vomiting. In some cases convulsions occurred. Death was usually preceded by acute respiratory distress or cyanosis.

The Australians *Bowden and French* found definite evidence histologically of tracheobronchitis, and acute bronchitis in twenty-nine of forty-three cases. The deaths occurred during the winter season, when respiratory ailments were at their height.

The striking similarity clinically and pathologically of some of the cases in our series (aLTB) to sudden death in infants is clear (tab. 1; 9).

Brigthon's report which includes a comparison of laryngotracheitis in chickens and fulminating aLTB in children is of interest, particularly in light of our cases of virus investigation. Both chicken and children showed a marked similarity in response to infection in the larynx and trachea. Both showed marked infiltration with mononuclear cells. This is characteristic of a tissue response to a virus disease rather than an acute infection from the hemolytic streptococci, the pneumococcus, and the staphylococcus. He reports the tracheal exsudate as showing degenerative cellular disease. *Beach* determined, in a series of bacteriological studies of the tracheal exsudates in fowls, that a filterable virus is present. On this basis, Brighton suggests that the acute fulminating LTB in children is a result of virus infection, with secondary invasions of the various bacteria found in the flora.

XII. Virus Considerations

The results of the viral research have already been referred to in the analyses of the bacteriology reports. An additional discussion of some important details now follows.

The single case of virus isolation of our series (tab. 1 no. 76) was clinically an LA form of aLTB with extensive involvement of the trachea and bronchi. The clinical picture was apparently a reflection of the secondary infection. The bacteriology revealed the primary virus agent, namely the influenza type A virus, as well as the Saprococci. The Saprococci are the non-hemolytic, non-green producing gram positive cocci. The blood picture examined two days after admission revealed a reactive leucocytosis. The antibiotic resistance tests revealed a weak group of reactions to penicillin, streptomycin, chloromycetin; and moderate reactions to the sulfanilamides, terramycin, aureomycin, and erythromycin.

Loeffler identified the virus as the influenza A strain. The Hirst test revealed corresponding antibodies to be present in the serum. The literature indicates the size of the virus to be 100—125 mu, differing with the strains used. The Hirst phenomenon is essentially the agglutinating power of the influenza virus on chicken erythrocytes. Other viruses besides the influenza virus can act similarly, however, this observation has had its greatest application in influenza investigations. The hemagglutinating

power is closely related to infectivity, and the ability of antiserum to neutralize virus is reflected in its inhibition of agglutination of erythrocytes in the presence of virus. The influenza strains are many and are of two groups, namely, A and B. Variation is great. One cannot definitely say if the time till the onset of the process in our case was prolonged, or if it acutely followed the initial infection with the virus. In this connection, the disease mechanism of the virus is of interest. Does the virus alone produce the disease, or is it the combination of the virus and another factor, as for example the Saprococci in this case, which initiates the disease process. In other words, is a mechanism existing in this case similar to that described by *Shope* in cases of the swine influenza? Has this case of aLTB a similar dual nature? Does the weather play a role as the exciting cause? These are etiological problems of influenza in general.

Loeffler states emphatically that no general conclusion can be made on the basis of this one case. One can only say that in one case of the LA form of aLTB the influenza virus type A was the primary etiological factor. One can speculate as to the relation to the other LA, LT, LTB forms of our aLTB cases. It has already been stated that our series shows other factors to be operating in aLTB, as well as a virus.

Clerf states that acute laryngotracheobronchitis (LTB form of aLTB) is not a specific entity but a clinical syndrome produced by a combination of factors. He considers it probably primarily influenzal in origin with secondary invaders complicating the clinical picture.

Baum is inclined to believe the basic cause of the disease to be the filterable virus of influenza, which in these cases causes a violent inflammatory reaction in the subglottic and tracheobronchial membranes and lays the groundwork for rapid subsequent invasion by the ever present streptococcus.

Gasser in discussing his cases of acute epiglottitis, finds the evidence directed against an assumption of primary virus etiology. The literature as well as our own experience here in Berne, is opposed to such a viewpoint, particularly in cases of acute epiglottitis (LA form of aLTB).

Influenzal convalescent serum should be included in the therapy. The results should provide a source of indirect etiological information.

We consider our cases of virus isolation and positive serology to support a contention that viral etiology is probably primary in a great number of cases of aLTB.

XIII. Allergic Considerations

The question of allergy and its etiological role in aLTB, if any, arose both during the course of our many analyses of our aLTB cases and following the extensive review of the literature of aLTB. The following is a summary of the attempt which was made to clarify the position of allergy in our cases.

In general, our allergy analysis was performed in two main steps: first, an attempt to find evidence to support a diagnosis of an allergic state, i. e. the determination to establish if hypersensitiveness was the cause of the presenting symptoms; and secondly, was evidence present to support a diagnosis of a specific allergen, i. e. the finding of the allergenic agent or agents responsible for the symptoms.

The attempt to diagnose the allergic state was considered of paramount importance, and found more material to work from than did the investigation in the second step. An allergic history was looked for in the presenting symptoms, the previous and family history. Concerning the presenting symptoms: —

1) No case showed the common manifestations of allergy including hay fever, asthma, eczema, migraine, urticaria, and angioneurotic edema. *Ellis* notes that it is reasonable to consider an allergic origin for any group of symptoms which recurs paroxysmally. In our series, ten cases showed repeat attacks, including four serious cases (no. 36, 39, 75, 77). However, in these repeat cases, no history or evidence of any allergic manifestations were reported.
2) In regards to environment, no evidence presented itself of the influence of the geographical location (rural or urban). Insufficient information was found in the histories to allow any conclusion to be made of the effect or presence of ingestants, inhalants, or contactants. A seasonal incidence was noted (tab. 2b). A greater degree of increased case incidence occurred in a change from warm to cold than from cold to warm weather. *Glanzmann* notes that in children showing an exsudative diathesis tendency, the occurrence of cold air (Polarluft) results in an acute inflammatory swelling of the subglottic respiratory mucosa and attacks of Pseudocroup. *Davison* in discussing subglottic allergic edema noted that some children subject to croup (any affection of the larynx or trachea accompanied by a hoarse, ringing cough and stridulous, difficult breathing) cannot sleep well in cold or well ventilated rooms without developing an attack. He considers this reaction a manifestation of allergy to the cold air. It would be of interest to learn what, if any, relationship exists between subglottic allergic edema and the LTB form of aLTB, as well as the role of cold in these two conditions. Specifically, does cold operate in some LTB cases as *Davison*

suggests it to operate in subglottic allergic edema? Are some LTB cases merely a further development of subglottic allergic edema? The existence of a definitely allergic case of LTB has been referred to by *Simmonds*.

3) *Kline* noted that a rapid onset of symptomatology, violent course and slow regression are characteristic of infections in allergic individuals. Many of our severe cases revealed such a clinical course (tab. 1). In general, it should not be presumed too strongly that the complaint is due to allergy because the patient has an allergic constitution. Here, the failure to find further evidence of allergy in the presenting symptoms or previous history prevents one from making any conclusion as to the reactive state of the patient.

Evidence of the previous and family history revealed no previous allergic condition, with the exception of one case (no. 8). This single case revealed a previous and family history of asthma. *Escher* notes the relative absence of asthma in our series, which one would not expect to be so striking in an affection having a possible allergic basis. Similarly, he notes that few asthmatics experience episodes of aLTB. In addition to the frank allergies, attention was directed to the presence of conditions of possible allergic origin which were possibly misdiagnosed as frequent "colds", "bronchitis", or "pneumonia". However, no basis was found to consider nineteen cases of our series showing recurrent episodes of catharrh as possible cases of asthma.

The findings of physical examination were those of the already mentioned respiratory obstruction syndrome. In all cases, the infectious, toxic nature of the process was of apparent paramount significance. The incidence of lymphatic involvement in our series was high. Of the total series, thirty-four cases, including eight serious cases, were those with tonsillar and adenoid hypertrophy and inflammation. Single cases were found of status thymolymphaticus and thymus hypertophy. A consideration here of the lymphatic involvement as an expression of an adaptation failure, in the sense of an allergy response, found no support in the material available in our series. On the basis of the literature, the lymphatic hyperplasia can be supported as an expression of an adaptation failure. However, *Escher* notes that in the overwhelming proportion of adeno- and tonsillectomized children with extensive lymphatic involvement, complications in the sense of aLTB incidents would be expected to show a much greater incidence, if such a mechanism were operating here. Furthermore, no apparent support is found for the importance attributed to focal infection in allergy. The apparent predisposition of pasty, puffy children with a lymphatic constitution has been noted. No clarification of its relation to allergy was found on the basis of the information available. Bronchoscopic examination revealed the extensive destruction described in our pathological considerations. In relation to the lymphatic involvement

and condition of the adrenal cortex, the autopsy findings, particularly in cases (no. 61, 27, 78) were considered of interest in relation to the adaptation syndrome.

On the basis of the laboratory procedures performed, no conclusion could be made concerning the question of allergy. Examination of the blood revealed an eosinophilia in eleven cases, including five serious cases (tab. 1). The significance of the eosinophilia is questionable due to the different time period which elapsed in the various cases between the onset of the process and the blood examination. As is noted in the literature, eosinophilia is characteristic but not pathognomonic of allergy. Reports of the bronchial secretion were regarded as inconclusive as to the presence of eosinophiles. Insufficient results of the sedimentation rate and an absence of nasal smear examination were found in our series.

Diagnosis for the presence of a specific allergen was not feasible in our cases.

One must conclude on the basis of our clinical material, review of the literature and classical concepts of allergy, that the conception of allergy as the primary etiological factor in some cases of aLTB found little definitive support in our series. The evidence in our series which could be cited to support a contention of allergy is considered too theoretical to allow any practical conclusions to be made at present. However in view of the inconclusiveness of our results, the feeling persists that studies should be performed to investigate the etiological significance of allergy in aLTB, particularly in the severe cases.

XIV. Summary and Conclusions

The purpose of this paper was to study the anatomical, physiological, clinical, epidemiological, and patho-anatomical material as presented in a series of eighty-six cases of acute laryngotracheobronchitis occurring in Berne during 1946 to July 1954. Special emphasis was placed on a group of twenty-eight (28) cases designated as severe, twenty-five (25) of which required tracheotomy and three (3) that died under conservative management. The following are the conclusions and summary based on this study: —

1. Clinically, acute laryngotracheobronchitis (aLTB) is a general, acute, infectious, non-diphtheritic, obstructive inflammation of the lower respiratory tract. It reflects itself in a clinical syndrome composed of the clinical forms laryngeal (LA) laryngotracheobronchitis, laryngotracheal (LT) laryngotracheobronchitis, and laryngotracheobronchial (LTB) laryngotracheobronchitis. The form and course depends on the site of chief involvement. In all cases the larynx, trachea, and bronchi are involved but in varying degree.

a. The pathophysiological relationship of the respiratory tract explain the greater incidence of LTB in the longer time intervals which elapsed prior to hospitalization, as compared to the LA cases which were predominantly found in the shorter time intervals.

b. The LT, and LTB cases show a greater similarity in their distribution during the time intervals elapsing prior to hospitalization than that of the LA cases. Substantiation is found for the clinical difficulty actually encountered in early diagnosis, particularly between the LT and LTB forms and less so between the LA and LTB forms.

c. If these different clinical courses, as reflected in the different forms of aLTB and their graphs bear a direct or indirect relationship to different or similar, multiple or single etiological factor(s) must remain on the basis of this study an open but still definite question.

2. Constitution and the reactive state of the individual patient influence the course and resultant clinical picture of the aLTB form.

a. Pasty, puffy, weak children with a lymphatic constitution apparently show a predisposition to aLTB. The greater tendency of tissue swelling in the pasty habitus is probably of special significance in aLTB.

3. Diagnosis should consist of a clinical and etiological phase.

a. Our concept of aLTB is a clinical one which suggests considering, particularly early in diagnosis, all the non-diphtheritic inflammatory obstructive infections of the lower respiratory tract as an actual or potential aLTB.

b. Of diagnostic importance is considered the positive indication in our series (based on the history, blood and bacteriology, and clinical course studies), of the activity of multiple agents in the development of aLTB. The difficulty at the onset of the diagnosis is believed due to failure to distinguish between the clinical and etiological (multiple) aspects of the diagnosis. At the onset of the diagnosis the problem is primarily clinical rather than etiological.

4. Concerning etiology: —

a. Etiological factors operating in aLTB may be categorized as primarily infectious or perhaps in single cases primarily constitutional determining infectious agents (a primary constitutional determining aLTB). The latter category increased in incidence in the LTB form.

b. The infectious etiology was paramount in all our cases.

c. We consider our cases of Influenza A virus isolation and positive serology to support a contention that viral etiology is probably primary in the majority of cases of aLTB.

d. Clinically, no association was found between an aLTB form and a particular blood picture. Etiologically, however, the variation in the distribution of the total and differential blood findings among the different aLTB forms, when considered together with the history, course, and bacteriological data of a particular aLTB form, could support a contention of multiple factors operating in aLTB.

e. No correlation was found to exist between the particular clinical course (LA, LT, LTB) and the reported bacterial flora. A similar flora was reported in all cases.

f. The conception of allergy as the primary etiological factor in some cases of aLTB found little support in our series. However, in view of the inconclusiveness of our results, it is suggested that suitable studies be performed to investigate the etiological significance of allergy in aLTB, particularly in the severe cases. It is possible that there exist mixed forms of allergic glottic and subglottic edema in which the addition of an infectious factor produces the severe character of the disease.

5. On the basis of the positive results of the viral research at Berne, it is suggested that these investigations be systematically instituted in all aLTB cases. In this manner additional evidence will probably be revealed to support a contention of primary viral etiology in most cases of aLTB.

6. Mortality: —

a. In general aLTB cases with longer histories prior to hospitalization showed a lower degree of mortality.

b. The high mortality of LTB is apparently limited chiefly to those LTB cases with an acute onset. However, of the ones with longer histories prior to hospitalization, the LTB form showed a greater incidence than did the LA or LT forms.

c. All the fatal LA cases presented an acute history of onset till hospitalization.

7. Therapy: —

a. In the main the therapy is primarily a supportive one, including antibiotics and tracheotomy with repeated bronchoaspirations when needed. It is suggested that the addition of Cortison in selected, severe toxic states, combined with intensive wide spectrum antibiotics would possibly provide an additional supportive measure, particularly in the primarily constitutional determining infectious aLTB cases.

b. Clinical improvement attributed to various antibiotics should take cognizance of the spontaneous remission of symptoms shown by some aLTB cases.

c. Bronchoaspiration followed by tracheotomy, upon the inserted bronchoscope was performed in all severe cases showing extreme toxicosis and dyspnea. Patients needing tracheotomy showed indications for it either immediately or a few hours after admission, regardless of the form of aLTB. This period represents the time of maximum evident toxicosis.

8. The seasonal distribution of aLTB cases revealed the lowest incidence during the month of June to August; the peaks in November to February.

9. The clinical evidence of our series does not exclude the possibility that in some cases the condition of spasmodic croup, LTB, sudden death in infants, and status thymolymphaticus may all be related, differing only in the degree to which the body adapted itself to a damaging insult.

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SEVERE CASES : DIVERSITY OF BACTERIA

Form alTB	Case No.	Streptococci								Neg. Rep.	Pneumococcus	B Proteus	B coli	H Infl.	Staphylo		SOOR	LEPTO	SAPRO	VIRUS
		Hemolytic Streptococci						Non-Hemolitic							albus	aureus				
		Hem.Strept.	A	B	C	D	E	Viridans	Enterococcus											
LA	42							42					42		42				42	
	28							28	28				28							
lT	59									59										
LTB	26								26							26				
	36a								36a											
	38						38						38		38					
	39a						39a	39a								39a				
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SUMMARY OF THE SEVERE CASES (tab. 1)

Jr. Nr.	Case No.	Name	Sex	Age	Period of Onset-Hospit.	Illness Hospit.-Tracheot.	Total Hosp.	History; Signs; Symptoms Prior to Tracheotomy
1013	63	W.R.	M	3½	1 day	Hrs.	7 days	Coryza cough, 2 weeks duration. Two days prior to admission, while eating, acute cough, cyanosis which subsided; later fever, stridor-insp. & expir; sweaty; anxious; muffled speech. Intensification of the above; increase of supra and infraclavicular retractions; pulse 130. Foreign body ruled out. Past history of hyperexcitability earlier in the year.
F_1 1398	75a	Z.W.	M	3	1 day	Immed.	3 wks.	Sudden onset in the night of dyspnea, fever. Emergency tracheotomy performed in the morning due to increasing symptoms of toxicosis & respiratory obstruction. Examination reveals extremely inflamed, enlarged, coated palatine tonsils; edema of the glottis, severe angina. Past history of difficulty in breathing since infancy, described as panting. Family history of asthma. No previous illness.
F_4 1521	56	T.M.	M	20mo	1 day	Hrs.	3 wks.	Severe, coarse cough 2 da. prior to admission. Diagnosed the next day as coryza by family physician. At night, fever 38, stridor, supra and infraclavicular retractions, dyspnea, paroxysms of cough and cyanosis. No response to conservative therapy during the night before and hrs. of the day of admission. Intensification of the above led to admission. History of LTB in cousin, who was visited one week before onset.
F_4 1530	57	B.W.	M	17mo	3 days	Hr.	17 days	Sudden onset of paroxysms of cough, with occasional vomiting 4 da. before admission. Admission due to increase in fever (39), anxiety, dyspnea, supra & infraclavicular retractions, insp. stridor & failure of conservative therapy. Bronchoscopy immediately performed. History of bronchitis and bronchopneumonia.

Instrumentation and Findings	Diagnosis Class.	Course	Laboratory Bacteriol.	Blood WC
ENT examination negative, upon tracheotomy, mucopurulent, brown secretion recovered in large quantities. Larynx-mucosa deep red, edematous, no membrane(s). Subglottic area not severely affected. Epiglottis and aryepiglottic folds thickened, acutely inflamed and edematous. MM show localized fibrin deposits.	LTB	Progressive improvement. Decanulation 4 da.later.	Staph.albus Staph.aureus Leptothrix	Low Reactive leucocytosis (normal)
Toxicosis exists prior to tracheotomy. Tracheo-bronchial mucosa edematous, fibrinous exudate.	LTB	Major improvement noted the second day,with decreasing pulse and respiratory obstruction. Decanulation 5 da. later.	?	Reactive leucocytosis,followed in a few days by an eosinophilia.
Repeated bronchoscopies revealed edema, adherent exsudate and crust formation of the laryngotracheaobronchial tree. Secretions aspirated, smear made. With increase of insp.stridor, pale cyanosis, pulse,respirations,dyspnea,-tracheotomy performed.	LTB	Gradual progressive improvement leading to decanulation 5 da. later.Bronchopneumonia treated. Possible atelectasis was believed present.	Saprococci	Reactive leucocytosis
Bronchoscopy reveals intensive inflammation of laryngotracheobronchial tree, with absence of pseudomembrane and suppuration. Secretions highly viscous. Tracheotomy performed and smear taken.	LTB	During tracheotomy operation cessation of respiration,followed by its resumption upon introducing the cannula. Progressive improvement, decannulation 6 da.later.	Enterococci Saprococci	Reactive leucocytosis, toxic granulations

Jr. Nr.	Case No.	Name	Sex	Age	Period of Onset-Hospit.	Illness Hospit.-Tracheot.	Total Hosp.	History; Signs; Symptoms Prior to Tracheotomy
F_4 659	58	F.W.	M	18 mo	3 days	Immed.	1 da.	During 4 da. prior to admission progressive increase of anxiety, dyspnea, fever (39.2), stridor, cough. Conservative therapy of local physician insufficient. Upon admission revealed exhausted child, pale cyanosis, stridor, respir. 60-70, fever 39. Immediate broncheoscopy and tracheotomy. History of upper respiratory infection with dyspnea of father 8 da. ago. No previous Illness.
F_2 1223	37	T.S.	F	3yrs.	Hrs.	Immed.	11 da.	Acute onset and progression the morning of admission, of fever 38, cyanosis, and dyspnea. Upon admission, pale cyanosis, unconscious, no exanthemata, perioral pallor, thorax retractions. A severe toxicosis. Patient never ill prior to present complaint. Family history negative.
F_2 1263	38	S.I.	F	1½	2 da.	Hrs.	13 da.	Crying onset 2 days ago attributed to "teething". Then cough, fever 37.2-39, increasing restlessness, sleeplessness, dyspnea, epigastric retraction, absence of cyanosis or pallor. No previous illness. No illness in family. Not vaccinated against diphtheria.
F_2 186	39a	H.R.	F	13mo	2 da.	Immed.	25 da.	Onset of fever 39.9-39, rhinitis with profuse nasal discharge. Night of admission awaken from sleep, with restlessness, hoarseness, a coarse ringing cough, inspiratory stridor. In clinic intensification of above symptoms plus thorax retractions, inspiratory and expiratory stridor. Inflammation of pharynx & larynx. Family history negative. First severe illness.

Instrumentation and Findings	Diagnosis Class.	Course	Laboratory Bacteriol.	Laboratory Blood WC
Anterior nasal examination reveals yellow-green crusts. Tonsils enlarged; not inflamed. Hypopharynx abundant, viscous, blood tinged with mucus. Neck-thyroid enlargement palpated. Direct laryngoscopy-edema, inflammation of larynx, maximum in subglottic area with fibrinopurulent exsudate. Following tracheotomy fibrinopurulent exsudate obtained; smear taken.	LTB	Improvement in respiration immediately following tracheotomy. Rapidly increasing toxicosis, despite a free airway, exitus, 4 hrs. later.	Strept. viridaus Entero-coccus	?
Bronchoscopy-edema, fibrinous punctation, inflammation of epiglottis, aryepiglottic folds and false cords. Epiglottis-markedly distended. Trachea free. Subglottic-minimal edema. Tonsils enlarged but not inflamed. Tracheotomy.	LA (LTB)	Progressive improvement with decannulation after 6 days	?	Low reactive leucocytosis
Laryngoscopy-epiglottis and aryepiglottic folds intensely enlarged, edematose. Vocal cords-adhesion posteriorly, thus presenting a U-formed opening. Trachea inflamed. Smear from larynx taken. Bronchoscopy: mass of purulent membranous material expelled.	LTB	Profuse purulent, fibrinous, membranose secretion received from tracheostoma for several days. Followed by progressive improvement and decannulation in 6 days.	Hemolytic Strept. Group E B.coli. Staph-albus.	reactive leucocytosis; toxic granulations; RBC: light anemia
Bronchoscopy- glottis and subglottic edema, involving vocal cords, no membrane. Tracheotemy-smear of bronchial secretions made; repeated aspiration of bronchi.	LTB	Improvement in case of respiration following tracheotemy. Up & downhill clinical course with episodes of paravertebral pneumonia, expiratory stridor, and appearance of pale cyanosis, dyspnea. Following sensitivity tests on flora terramycin used. Gradual improvement; decannulation 11 da. post.op.	Hemolytic Strept. Group E; Strept. viridaus Strept. aureus	reactive leucocytosis

Jr. Nr.	Case No.	Name	Sex	Age	Onset-Hospit.	Hospit.-Tracheot.	Total Hosp.	History; Signs; Symptoms Prior to Tracheotomy
F_2 27	55	S.E.	F	2yr	1 da.	Immed.	4 weeks	Ringing, coarse cough in night prior to day of admission, followed in morning by fever 38.5, panting. Conservative therapy inadequate. Signs of toxicosis and an acute edema of tracheobronchial mucosa present upon admission. Family history of adute rhinitis in mother as well as neighborhood at present.
F_2 1426	60	P.R.	F	3yrs	1 da.	Immed.	Hrs.	Thirst at night followed in A.M. by rapidly increasing dyspnea. Admitted with severe dyspnea, cyanosis, supra & infra clavicular retractions progressing to loss of pulse and elimination of respiratory excursions. No history of previous illness.
F_4 1326	61	B.B.	F	20mo	1 da.	Immed.	Hrs.	Unexplained fever onset 1 week ago followed during next day by acute onset of diarrhea, and later vomiting, dyspnea, fever 39.9, swallowing difficulty, pallor of face, hoarseness. Admission revealed extreme toxicosis, stridor, extreme livid cyanosis, glottis and subglottic edema. History of tuberculosis in area, pertussis.
F_2 152	36a	D.J.	M	2yrs	3 hr.	Immed.	18 da.	Acute onset of dyspnea, pallor, progressing to severe toxicosis, unconsciousness upon admission. Routine examination reveals bronchial involvement, constricted pupils, dyspnea, thorax tretractions, sweating. Negative history of previous illness.

Instrumentation and Findings	Diagnosis Class.	Course	Bacteriol.	Laboratory Blood WC
Bronchoscopy-trachea and bronchi intensely red, false membrane. Immediate tracheotomy. Smear of bronchial secretion made.	LTB	Dramatic improvement with improved facial color, normal respirations. Progressive improvement of bronchopneumonia and decannulation 11 da. later.	Staph. albus hem. Staph. aureus hem.	?
Immediate tracheotomy, reveals acute obstruction in tracheobronchial tree.	LTB	Exitus. No section.	?	?
No inflammation seen in oral cavity, tonsils, posterior pharyngeal wall. Laryngoscopy; intense red, edematous epiglottis and aryepiglottic folds. Bronchoscopy; edema, inflammation of tracheobronchial tree. Repeated bronchial aspiration results in temporary relief. Tracheotomy followed.	LTB	Exitus one hour after tracheotomy. See section	Hemolytic streptococci	?
Laryngoscopy-purulent secretion. Difficult to observe any details. Tracheotomy produced an immediate improvement, but occasional Cheynes-Stokes respiration.	LTB	Critical status for following 2 days, with increased tempt., tachypnea, broncho-pneumonia, profuse tracheal secretion. On basis of antibiotic resistance tests of tracheal secretion, chloromycetin substituted for penicillin and streptomycin. Fever declined. Is temp. decline the specific action of chloromycetin or an expression of LTB. Develop. of cutaneous emphysema of thorax.	Enterococci	Reactive leuco-cytosis. Increased Eosinophiles; lymphocytosis.

Jr. Nr.	Case No.	Name	Sex	Age	Period of Illness Onset-Hospit.	Hospit.-tracheot.	Total Hospit.	History; Signs; Symptoms Prior to Tracheotomy
F_2 1339	40	J.A.	F	7mo	2 da.	Hr.	3 weeks	Increasing stridor, dyspnea leading to admission. In clinic shallow respirations, extreme toxicosis, pallor. Negative family history. First severe illness.
F_2 353	41	B.V.	M	3yrs.	3 da.	Immed.	9 da.	Rash of measles followed 2 days later by ringing cough, dyspnea. Day of admission increasing dyspnea, vomiting, developing cyanosis. In clinic, severe toxicosis, insp.& expir. stridor, cyanosis. Measles in family at present; onset 2 weeks ago in a sister.
F_2 639	77a	N.J.	M	4mo	2 da.	5 hr.	11 wks.	Acute coryza with ringing cough, signs of laryngeal stenosis increasing in severity during a 2 day period. In clinic stridor, blue cyanosis replaced by pale cyanosis, severe toxicosis. Father had pseudocroup when a child of 3 years. No illness in family. First serious illness.
F_4 1386	59	H.H.	M	8mo	3 da.	Immed.	10 da.	Sudden onset of dyspnea, cyanosis leading to admission. Fever 38.2 pulse 160. Examination of mouth and larynx reveals mucus and false membrane formation. History of previous illness negative.
F_2 526	53	B.M.	F	18mo	8 da.	2 da.	3 wks.	Rhinitis, cough, vomiting and diarrhea progressing to dyspnea, stridorose breathing, fever 38.4. 4 da. prior to admission. Conservative therapy inadequate. Family history of death of 12 month old sister. from "laryngitis". Tracheotomy performed. Brother at present has pleurisy. Patient never ill previously.

Instrumentation and Findings	Diagnosis Class.	Course	Laboratory Bacteriol.	Blood WC
Bronchoscopy; extreme inflammation, edema, fibrinous membrane particles in larynx presumed to be of tracheal origin. Entire tracheobronchial tree injected, edematose, and coated with fluid, purulent exsudate. No membrane production. Tracheotomy-immediate improvement in respiration.	LTB	Progressive improvement & decannulation 10 da. post-op.	?	?
Laryngoscopy; severe inflammation and edema of laryngeal mucosa. Localized areas of fibrinous exsudate on tracheal lining. Immediate tracheotomy. Tracheotomy repeated aspirations with occasional improvement.	LTB	Critical clinical course in 24 hr. period post.op. From second day post.op. progressive improvement. Decannulation 6 da. post.op.	?	Leucopenia with Eosin 5%
Bronchoscopy; tracheobronchial secretions following tracheotomy. Fever maintained over 3 da. post.op., accompanied by mucus rich, green stools. Condition improved thereafter presenting indications for decannulation 5 da. post.op.	(LTB)	First decannulation attempt followed by stridor, cyanosis, fever 38,-a repetition of initial symptomatology. Second attempt 7 da. post.op. led to slight breathing difficulty. Third attempt-3rd wk. post.op. successful, however, while drinking fluid acute episode ensued. 4th attempt-5th wk. post.op. unsuccessful. Attempt at removal of cannula for short periods finally successful, however accompanied at start by acute symptoms of resp. obstruction & frequent cannula changes.	Staph. aureus Enterococci Strept. viradans	?
Immediate bronchoscopy markedly eases respir. Upon removal of bronchoscope, dyspnea ensues. Subglottic swelling. Tracheotomy followed.	LTB	Repeated fibrino purulent discharge from tracheotomy cannula, followed by liquifaction & improvement 2 da. later. Decannulation after 6 da.	Negative smear.	Within norm. Toxic granulations.
Oropharynx reveals large, inflamed tonsils and profuse, viscous, frothy secretion. Bronchoscopy-rich fibrinous exsudate fills entire bronchial tree. Due to varied clin. course, tracheotomy delayed 2 da. until indications.	LTB	Progressive improvement; decannulation 6 da. later.		Reactive leucocytosis.

Jr. Case No.	No.	Name	Sex	Age	Period of Onset-Hospit.	Illness Hospit-Tracheot.	Total Hospit.	History; Signy; Symptoms Prior to Tracheotomy
F_2 1062	27	K.M.	F	13mo	2 da.	Hrs.	Hrs.	Hoarseness, labored breathing, cyanosis varying in intensity during a 2 day period. Upon admission aphonie ; severe toxicosis, pale cyanosis, thorax retractions. Family and personal history negative.
F_2 1328	42	E.M.	M	2½yrs	1 da.	Hr.	19 da.	Coarse, ringing cough with gradual development of severe dyspnea, fever 39, cyanosis. Immediate tracheotomy performed. No illness in family at present. Previous illness; pertussis. First episode of resp iratory difficulty.
F_2 96	33	K.H.	M	3 yr.	3 da.	Hr.	16 da.	Fever, cough, hoarseness with developing difficulty in breathing. Flucuation in severity until shortly before admission acute onset of pallor, thorax retractions. In clinic dilated pupils, very shallow respirations, severe toxicosis. Repeatedly treated for bronchitis.
F_2 1226	73	B.U.	M	lyr. & 11mo.	3 da.	12 hr.	13 da.	Onset of coryza followed by fever, increasing malaise, hoarseness. Day of admission acute onset of fever 40, dyspnea, dry and racking cough. Conservative treatment ineffective; admission. In clinic nasal mucosa inflamed, increasing dyspnea, stridor during physical examination. Observed 12 hr. before tracheotomy. No previous illness. Twin brother at present has laryngitis and bronchitis.

Instrumentation and Findings	Diagnosis Class.	Course	Laboratory Bacteriol.	Laboratory Blood WC
Bronchoscopy; fibrinosis, neurotic laryngitis. Tracheobronchial passages free. General inflammation of post. pharyngeal wall. No membranes.	LA (LTB)	Upon opening the trachea, a sudden cessation of respiration. Exitus.	?	?
Bronchoscopy; fibrinose, necrotic laryngitis. Trachea-inflamed, edematose, crusted, extending to bronchi. Tracheotomy; smear made of tracheo-bronchial secretions.	LTB	Despite improvement in respir. following tracheotomy, a protracted clinical course with severe bronchitis. Decannulation 11 da. post.op.	Strept. viridans B.coli Staph. albus Saprococci	Reactive leucocytosis followed in a few days by an eosinophilia
Bronchoscopy; intensive subglottic swelling. Trachea and bronchi free. Tracheotomy; followed by improvement in skin color.	LT (LTB)	Progressive clinical improvement & decannulation 11 da. post. op.	?	7000 WC Eosin 6%. Slight anemia (Aniscocytosis; poikylocytosis). Lymphocytosis.
Bronchoscopy; subglottic edema extending to trachea and bronchi. Tracheotomy; followed by immediate improvement. Smear of tracheobronchial secretions made. Repeated bronchoscopies performed and aspirations with recovery of massive, viscous, purulent material.	LTB	Progressive improvement following tracheotomy with decannulation 5 da. post.op.	Staph. aureus Strept. viridans. Enterococci. B. proteus. Saprococci.	?

Jr. Nr.	Case No.	Name	Sex	Age	Period of Illness Onset-Hospit.	Hospit.-Tracheot.	Total Hospit.	History; Signs; Symptoms Prior to Tracheotomy
F_2 122	74	K.M.	F	3yr	4 da.	15 da.	18 da.	Ringing cough, deep voice, fever, which responds to conservative treatment. 10 days previously, mild coryza. Night and day before admission recovery of above with conservative cough with chest pain. Impression of influenza pneumonia and conservative treatment including terramycin. Progressive increase in dyspnea, fever 38-39, restlessness, cyanosis, dehydration. In clinic unconscious, severe toxicosis, narrow pupils, inspir. & expir. stridor, thorax retractions, pulse 140. Immediate instrumentation. First episode of respiratory obstruction. Sister and brother at present ill with grippe. Physician noted absence of secretions in patient at onset in contrast to his brother and sister.
286	76	B.T.	F	2yr.	Hrs.	2 hrs.	12 da.	Upon awakening fever 39, afternoon panting, slight rhinitis with inspiratory stridor and thoracic retraction pale cyanosis. Upon admission immediate instrumentation. Previous illness: measles, pertussis. Family history negated.
F_2 133	78	G.H.	M	6yr.	1 wk.	hr.	4 da.	Coryza, ringing cough, difficult respirations for 1 week prior to admission. Night before day of admission, onset and progression of dyspnea, thorax retractions. In clinic, pale cyanosis, distended neck veins, respir. & expir. stridor. Immediate instrumentation. No previous illness or illness in family at present.

Instrumentation and Findings	Diagnosis Class.	Course	Laboratory Bacteriol.	Blood WC
Laryngoscopy; Bronchoscopy; massive crust formation in laryngo-trachec-bronchial passages. During aspiration, period of apnoe arose. Immed. tracheotomy followed. Smear of tracheobronchial material taken.	LTB	Critical course for 9 da. post. op. Repeated aspiration and removal of secretions and crusts. Fever disappeared 9 da. following admission. Decannulation 15 da. post. op.	Hospital. Da. 1 Crusts: Staph. aureus Enterococci Strept. Viridans. Da. 4-Bronchial secretion Staph. aureus Enterococci Strept. viridans Yeast Da. 5-Tracheobronchial & crusts. Same as Da. 4	R.L. Lymphopenia
Bronchoscopy; Laryngoscopy; - intense edema, inflammation of supraglottic structures. Diagnosis of epiglottis. Tracheotomy; -during procedure, period of apnea with recovery. Some membrane found. Smear taken.	LA	Momentary relief but continued critical course for 1 da. post. op. with dyspnea, aspiration of thick, tenacious, gran tracheobronchial secretions, fever. Improvement 2-4 days post. op. Reappearance of fever combated successfully with synthomycetin. Decannulation 6 da. post. op.	Influenza virus Saprococci	Low reactive leucocytosis
Bronchoscopy; Laryngoscopy; vocal cords area edematose, inflamed, fibrinous coat. Bronchi-bilaterally clogged with fibrinose, tenacious, viscose secretion. Tracheotomy-processes pyramidales present. Smear taken. Immediate improvement. Venous blood sample for virus study.	LTB	Critical course with pneumonia, diarrhea, fever 40, repeated bronchoscopies and aspirations and continous production of crusts in trachea and bronchi. Exitus on 4th hospital day.	Bacteremia Staph. aureus	Low reactive leucocytosis; Lymphopenia

Jr. No.	Case No.	Name	Sex	Age	Period of Illness Onset-Hospit.	Hospit.-tracheot.	Total Hospit.	History; Signs; Symptoms Prior to Tracheotomy
459	79	F.A.	F	3yr.	1 da.	Hr.	9 da.	Onset with cough progressing to stridor believed due to pharyngitis. In clinic clear voice, some inspiratory stridor. Immediate instrumentation on basis of throat examination revealing severe edema, inflammation of epiglottic folds. No previous illness or illness in family at present.
F_2 548	26	S.M.	F	11mo	1 da.	--	18 hr.	Increasing fever, dyspnea of 1 day duration. Admission-respiratory & expiratory stridor; fever 41.2; bronchitic rales upon auscultation; extreme cyanosis. No previous illness; no family illness at present.
F_2 449	28	B.W.	M	7wks.	1 wk.	--	18 hr.	Acute coryza responding to antibiotic and conservative therapy until onset of repeated paroxysms of dyspnea in night and morning of admission. Clinic-pale cyanosis; clear cry; diagnosis of free larynx; and tracheal obstruction with paroxysmal severe dyspnea. No previous illness; no family illness at present.
F_2 412	51	S.H.	M	7yrs.	1 wk.	--	24 hrs.	Upper respiratory infection admission to pediatrics; development of profuse purulent exsudation with dyspnea; fever 38-39; nasal crusts.

Instrumentation and Findings	Diagnosis Class.	Course	Laboratory Bacteriol.	Blood WC
Bronchoscopy; Laryngoscopy;- edematous, inflamed epiglottis and aryepiglottic folds. Entrance to larynx slitlike. Vocal cords not visible. Tracheotomy; - subglottic edema. Deeper bronchial areas free.	LA (LTB)	Progressive improvement, and decannulation 6 da. post. op.	?	Reactive leucocytosis
Laryngoscopy 1-some supraglottic and subglottic edema; no membrane. 2-despite edema, airway is suffciently wide. Throat smear taken.	LTB (Bronchiolitis)	Progressive, fulminating course with fever 40-41.8; increasing dyspnea; circulatory collapse; death 18 hrs. after admission.	Strept. viridans Staph. aureus	?
X-Ray;-tracheal compression. Examination reveals tracheal obstruction.	(LTB)	Progressive increasing paroxysms of dyspnea. Clinical impression of non-involved larynx. Exitus 18 hrs. after admission.	Smear from Spleen:- Enterococci B. coli Atypical B. coli	Reactive leucocytosis; toxic granulations; neutropenia.
Oral cavity, tonsils; meso-, epi-, hypopharynx; larynx covered with viscous, purulent material. Ulcerations on tongue.	LTB	Progressive sepsis with toxicosis. Exitus.	?	?

SUMMARY OF PATHOLOGICAL FINDINGS IN THE AUTOPSIED CASES OF OUR SERIES (tab. 9)

Case	Gross Findings	Microscopic Findings: Upper Respiratory	Microscopic Findings: Lung
58 S.Nr. 200/48	Fibrinous laryngotracheitis; larynx edema; moderately enlarged cervical nodes; purulent bronchitis; status after tracheotomy; acute splenic tumor; well developed thymus; normal pharynx and esophagus; massive subglottic edema covered with glassy, tenacious, muccoid material; narrowed tracheobronchial passageways.	Larynx; -epithelial mucosa locally desquamated; replaced with fibrinous exsudate; tunica propria edematose, infiltrated with poly.leuco., lympho; vessels congested and distended. Trachea; -glassy, viscose, mucoic, tenacious plugs; MM edema, congestion; Tracheostoma below the cricoid cartilage.	Areas of normal, atelectatic, and emphysematous parenchyma with some interalveolar septal rupture; septal capillary congestion; purulent bronchitis.
61 S.Nr. /49	Edema, congestion, fibrinous exsudate in the larynx and trachea; glottis edema; lung emphysema; acute splenic tumor; status after tracheotomy.	Congestion, edema, fibrinous exsudate in larynx and trachea. Tracheostoma; free respiratory lumina.	Emphysema; acute interstitial pneumonia.
27 S.Nr. 321/52	Fibrinous, necrotic, laryngitis; status after tracheotomy; status thymolymphat; patent foramen ovale; auricular dilation; pleural hemorrhage; acute splenic tumor; kidney, liver congestion.	Waldeyer lymphatic ring massively enlarged; pharynx, larynx, trachea edema and congestion increasing toward the bronchi; aryepiglottic folds edematose; slitlike glottis opening. Larynx MM: -focal infiltration of poly-leuc; lympho-plasma cells; few eosinophils.	Areas of normal, emphesematous, -atelectatic, congested, edematous parenchyma; interalveolar septal rupture; septal capillary congestion; purulent bronchitis; pleural hemorrhage.
28 S.Nr. 174/53	Acute laryngitis; pale edema of pharynx, larynx, retropharynx; lung congestion; subpleural hemorrhage; acute splenic tumor; small thymus; stomach, duod., colon edema.	Congestion, edema of the larynx & pharynx; epiglottic edema, infiltration of poly.leuc; lympho; single plasma and eosin.cells; periglottic fibrous tissue edema.	Bilateral purulent, serofibrinous pleuritis; lobular fibrinous pneumonia; lung edema; congestion; bronchi; -local dilatation and exsudate with poly.leuc., eosin. B acteria in necrotic material.
78	Dilatatio cordis; splenic enlargement; status after tracheotoma; larynx edema; tracheobronchial-crusts; thymus moderate.	Larynx edema; necrotic fibrino-purulent tracheobronchitis; plica aryepiglottica-edema, congestion; trachea-local ulceration and necrosis.	Congestion; subpleural hemorrhage.

Other Significant Findings	Cause of Death
Myocard;-extreme edema, congestion, of the interstitial connective tissue. Stomach-edema; congestion of the mucosa. Liver:-edema; gross, yellow, surface punctations; cloudy swelling; diffuse fatty change. Kidney:-cloudy swelling. Brain:-edema; congestion.	Acute fibrinous "grippe" laryngotracheitis and purulent Bronchitis with sepsis.
Acute splenic tumor; generalized cloudy swelling in the parenchyma of the vital organs.	Severe toxicosis accompanying an acute "grippe" laryngotracheitis; acute sepsis of possible pneumococcal origin.
Adrenal cortex:-hypertrophic; lipoid deficient; cloudy swelling. Myocard. and kidney:-cloudy swelling. Spleen; mesenteric; intestinal; cervical lymphnodes; Hyperplasia of splenic follicles and nodes.	Acute necrotic, fibrinous laryngitis; Status thymicolymphaticus; circulatory collapse.
Cloudy swelling of the kidney and liver. General anemia.	Supraglottic laryngitis with acute edematose stenosis asphyxia. Etiology:-role of allergen to be considered.
Cloudy swelling of myocardium, liver, kidney. Chronic splenitis. Kidney:-parenchymal hemorrhage. Adrenal cortex:-lipoid depletion; stage of exhaustion. Liver:-peripheral fat deposit. Brain:-cerebral edema.	Laryngotracheobronchitis